PHARMACY AND POISONS BOARD
HONG KONG
香港藥劑業及毒藥管理局

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6th November 2024

To: Certificate holders of registered pharmaceutical products

Dear Sir/Madam,

New Warnings for Isotretinoin

The Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee (the Committee) under the Pharmacy and Poisons Board has considered, in its meeting on 31st October 2024, the latest warnings regarding the risk of psychiatric disorders and sexual dysfunction in patients taking systemic isotretinoin by the drug regulatory authorities of Canada, Singapore and the United Kingdom, and decided that the sales pack labels and / or package inserts of all registered products containing isotretinoin shall include the following new safety information (or equivalent [Note 1]) as appropriate:

> ***"Special Warnings and Precautions for use***
>
> *Psychiatric disorders*
> *Depression, depression aggravated, anxiety, aggressive tendencies, mood alterations, psychotic symptoms, suicidal ideation, suicide attempts and suicide have been reported in patients treated with isotretinoin.*

Note 1 Related safety information with other wording in accordance with reputable references and/or approved package inserts from drug regulatory authorities of reference countries may also be accepted on a case-by-case basis.

Patients, and where appropriate, parents or carers, must be counselled about the risk of psychiatric adverse events with isotretinoin prior to prescription of isotretinoin, and preferably prior to any referral that might include consideration of isotretinoin treatment.

All patients should have an assessment of their mental health before starting treatment with isotretinoin and be assessed regularly during treatment for developing or worsening psychiatric disorders. Particular care needs to be taken in patients with a history of depression. Patients should be referred for appropriate psychiatric treatment if necessary. Discontinuation of isotretinoin may be insufficient to alleviate symptoms and therefore further psychiatric or psychological evaluation may be necessary.

Awareness by family or friends may be useful to detect mental health deterioration.

Sexual Disorder

Isotretinoin use may be associated with sexual dysfunction. There have been reports of long lasting sexual dysfunction where the symptoms have continued despite discontinuation of isotretinoin.

Patients, and where appropriate, parents or carers, must be counselled about the risk of sexual dysfunction with isotretinoin prior to the prescribing decision, and ideally prior to any referral that might include consideration of isotretinoin treatment. The age and maturity of the patient should be taken into account in choosing the most appropriate counselling approach, including giving the option to discuss without parents or carers present where appropriate.

All patients should be asked about the presence of symptoms or signs of sexual dysfunction prior to starting treatment with isotretinoin, and monitored for the development of new sexual disorders during treatment.

Undesirable effects

'Aggressive tendencies, anxiety, mood alterations' are listed under 'Psychiatric disorders' with frequency 'Rare'.

'Psychotic disorder, abnormal behaviour' are listed under 'Psychiatric disorders' with frequency 'Very rare'.

'Depression, depression aggravated, suicide, suicide attempt, suicidal ideation' are listed under 'Psychiatric disorders' with frequency 'Not known'.

'Sexual dysfunction including erectile dysfunction and decreased libido, gynaecomastia, vulvovaginal dryness, orgasm abnormal, genital hypoaesthesia' are listed under 'Reproductive system and breast disorders' with frequency 'Not known'."

You are therefore required to ensure the sales pack labels and / or package inserts of the concerned products registered by your company contain the above safety information to comply with the new requirements. In addition, you are reminded to ensure the sale pack labels and / or package inserts of the registered metformin products already contain the safety information stated in the Annex (or equivalent [see Note 1 above]) as previously endorsed by the Committee. Please submit application for the change of the registered particular(s) to the Drug Office via the online Pharmaceutical Registration System 2.0 (PRS 2.0) at www.drugoffice.gov.hk/prs2-ext/client_authentication.jsp for approval within 2 months from the date of this letter. Failing to comply with the above requirements may result in de-registration of the products or registration not being renewed by the Committee upon certificate expiry.

For further enquiries on the registration matters of pharmaceutical products, please contact the Drug Office at 3974 4175.

Yours faithfully,

(Y. F. YEUNG)
Secretary,
Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee

c.c. 7-15/3, Product Files

Annex

Safety information previously endorsed by the Pharmacy and Poisons (Registration of Pharmaceutical Substances: Certificate of Clinical Trial/Medicinal Test) Committee

For all isotretinoin-containing pharmaceutical products:

(a) The safety information related to the risk of severe skin reaction. Example of wording as follows:

"There have been post-marketing reports of severe skin reactions (e.g. erythema multiforme (EM), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)) associated with isotretinoin use. As these events may be difficult to distinguish from other skin reactions that may occur, patients should be advised of the signs and symptoms and monitored closely for severe skin reactions. If a severe skin reaction is suspected, isotretinoin treatment should be discontinued."

Additional requirements for the supply of Isotretinoin products

(a) A patient information leaflet, in both Chinese and English, should be provided in each package of the product highlighting the teratogenic effect of the product.

(b) A letter to be sent to all doctors to whom the product is supplied, to advise them of the teratogenicity of the product and the precautions associated with the use of the product, and that the product should only be supplied to patients along with the above-mentioned patient information leaflet.

(c) Consent forms should be provided to the doctors who should also be asked to ensure that patients sign the consent forms before being supplied with the product, the signed forms to be kept by the doctors to maintain patient confidentiality.